

# THE REGENERATIVE CAPACITY OF MAMMALIAN HEART MUSCLE

BY

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King in 1940, in this journal, described appearances that he believed to be those of myocardial regeneration in a case where death had occurred four days after a stab wound of the chest. A review of the literature, however, shows the opinion most generally held is that hyperplasia of cardiac muscle does not occur. Another consideration prompted the present study: Le Gros Clark (1946) showed that considerable regeneration of skeletal muscle took place in the rabbit following experimental injury. It therefore seemed desirable that the regenerative power of the rabbit myocardium should be studied.

## METHODS AND RESULTS

It is very difficult to produce by crushing comparable lesions in rapidly beating hearts, and as burning had been employed successfully by Thomas and Harrison (1944) for functional recovery tests in rats, it was decided to use this type of lesion.

In adult rabbits the heart was exposed under anaesthesia, with full aseptic precautions, and a severe burn made in the lower third of the left ventricle by the application of the head of a nail, 5 mm. in diameter, heated to a dull redness. The chest wound was closed and the animals allowed to survive for periods ranging from 3 days to 3 months. The hearts were then examined microscopically.

The appearances in the injured area were at first simply those of severe inflammatory reaction with destruction of tissue. Later a progressive organization into scar tissue occurred; but there was no evidence of regeneration of cardiac muscle.

At first the site of injury showed as a deep crater (Fig. 2) filled with fibrin clot and necrotic tissue to which pericardial adhesions had become attached. Surrounding this was an area containing damaged muscle fibres invested by macrophages of different kinds. Amongst these cells monocytes were prominent (Fig. 4), a point which has been noted by

pathologists in acute muscle infections generally. The damaged muscle fibres showed fragmentation (Fig. 5), the lines of cleavage seeming to be at the intercalated discs, and their transverse striations and nuclei stained less strongly. Very early on there were great numbers of fibroblasts to be seen within the injured area which was soon invaded by capillaries from the neighbouring healthy tissue (Fig. 1). After a month there was a clear line of demarcation between undamaged muscle and scar tissue (Fig. 3) although here and there fragments of muscle with attendant phagocytes could still be seen. At no stage was sprouting of myoblasts detected: nor were mitotic figures found, although it must be admitted that Le Gros Clark (1946) found nuclear division took place as a general rule by amitosis in regenerating skeletal muscle. The longitudinal splitting of fibres described by King (1940) was not observed.

## DISCUSSION

Compared with skeletal muscle cardiac muscle is much less easy to trace in serial sections, but even so it is felt that no signs of regeneration were missed. The explanation of the difference in regenerative capacity of the two classes of muscle, as shown in the rabbit, may be histological, or it may be that in the heart rest cannot be enjoyed by the damaged fibres. Distinguishing features of cardiac muscle are the ill-defined or absent sarcolemma, centrally placed nuclei, branching fibres, well marked longitudinal striation, granular sarcoplasm which somewhat masks the transverse striations, and the presence of intercalated discs. It is usually stated that there is continuity of myofibrils through the discs. Fig. 6 shows this, but I am not satisfied that such continuity exists through all discs and it may be that the discs, whatever their physiological significance may be, act as an impediment to regeneration. It might be argued that burning is

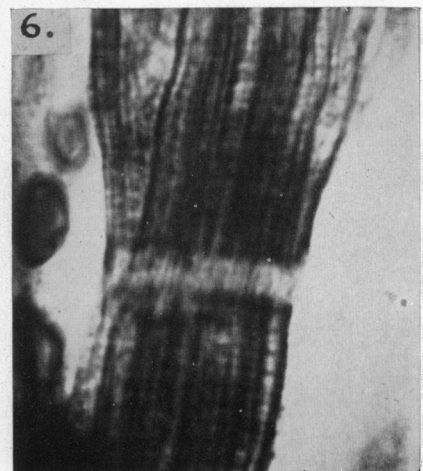
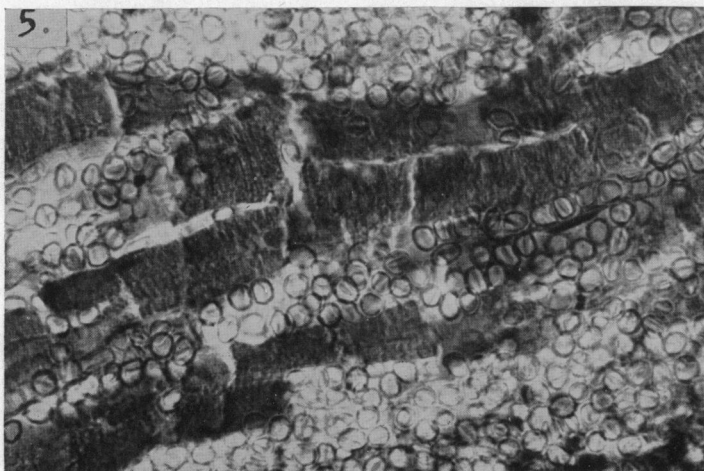
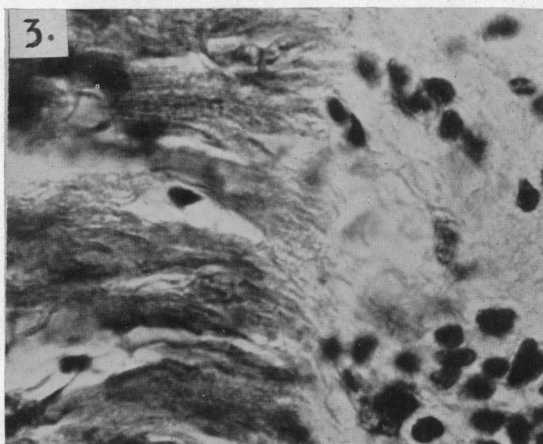
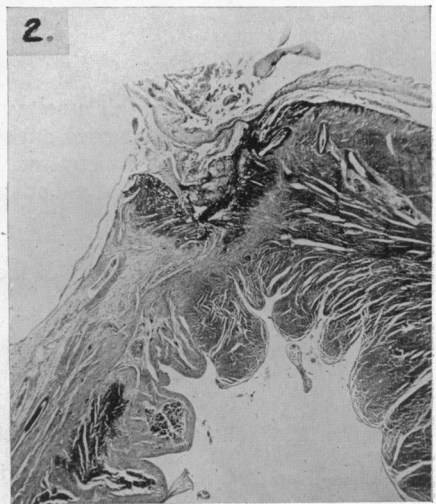


FIG. 1.—Section 1.2.3. of rabbit heart (R.7) three days after operation. Healthy fibres above and to left. Numerous fibroblasts are shown within the damaged area which is becoming revascularized. Magnification:  $\times 500$ .

FIG. 2.—Section 32.2.3. of rabbit heart (R.4) seven days after operation. A general view of the crater produced by the burn is shown. Magnification:  $\times 7$ .

FIG. 3.—Section 3.2.2. of rabbit heart (R.10) one month after operation. Healthy tissue to left, scar tissue to right. The line of demarcation is sharp. Magnification:  $\times 650$ .

FIG. 4.—Section 32.2.3. of rabbit heart (R.4) seven days after operation. Damaged myocardial fibres are shown surrounded by great numbers of phagocytes. A large monocyte is especially pronounced. Magnification:  $\times 530$ .

FIG. 5.—Section 1.2.3. of rabbit heart (R.7) three days after operation. To show fragmentation of the muscle fibres. Magnification:  $\times 650$ .

FIG. 6.—Section of undamaged rabbit heart muscle. To show continuity of myofibrils through an intercalated disc. Magnification:  $\times 1375$ .

too severe a lesion for a fair assessment of results, but Harrison (1947) who carried out similar experiments also showed that skeletal muscle in rabbits did regenerate after burning by diathermy.

#### SUMMARY

Following experimental injury of the rabbit heart

by burning there is no evidence of regeneration of cardiac muscle.

To Professor C. M. West, University College, Cardiff, in whose department this work was started, and to Professor John Kirk, my present chief, I wish to express my gratitude for much helpful advice. The photomicrographs are the work of Mr. S. R. Scarfe.

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